Patient leaflet in accordance with the Pharmacists' Regulations (Medicinal Products) - 1986

This medicine is dispensed with a doctor's prescription only

Mercaptizol

Tablets

Active ingredient
Each tablet contains:
methimazole 20 mg

Inactive ingredients and allergens: see section 2 under 'Important information about some of this medicine's ingredients', and section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about the medicine. If you have any further questions, consult your doctor or pharmacist.
This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

For the treatment of hyperthyroidism.

Therapeutic group: sulfur-containing imidazole derivative.

2. Before using this medicine

Do not use this medicine if:

- You are hypersensitive (allergic) to the active ingredient methimazole or to any of the other ingredients in this medicine (see section 6 'Additional information').

Special warnings about using this medicine

- **Congenital malformations.** Mercaptizol may cause fetal harm, particularly when taken in the first trimester of pregnancy (see section 'Pregnancy and breastfeeding').
- **Agranulocytosis** (severe deficiency of white blood cells called neutrophils). A potentially life-threatening side effect of Mercaptizol therapy. Immediately report to your doctor any symptoms suggestive of agranulocytosis, including fever, sore throat, headache, rash or general malaise. Pay special attention when you are taking other medicines which may cause agranulocytosis. Leukopenia (decrease in the number of white blood cells – Leukocytes), thrombocytopenia (decrease in platelets), and aplastic anemia (decrease in blood cell count) may also occur. Discontinue treatment and contact your doctor in the presence of agranulocytosis or

aplastic anemia (see also section 4 'Side effects'). The doctor may refer you to tests to monitor your bone marrow indices.

- **Hepatotoxicity.** There have been reports of hepatotoxicity (including acute liver failure) associated with Mercaptizol therapy. The risk of hepatotoxicity appears to be lower with Mercaptizol than with propylthiouracil, another medicine for hyperthyroidism, especially in children. Symptoms suggestive of a liver problem (anorexia, pruritus, right upper quadrant abdominal pain, etc.) require immediate evaluation of liver function (bilirubin, alkaline phosphatase) and hepatocellular integrity (ALT, AST tests). In case of a liver function abnormality, your doctor may instruct you to stop the treatment with the medicine (see also section 4 'Side effects').
- **Hypothyroidism**. Mercaptizol may cause hypothyroidism, necessitating routine monitoring of thyroid hormone levels (TSH, free T4) with adjustments of medicine dosing to maintain euthyroid state.

If you need to undergo any surgery (including dental surgery) or urgent treatment, inform the doctor that you are taking Mercaptizol.

- **Vasculitis (inflammation of blood vessels).** Cases of vasculitis resulting in severe complications have been reported in patients treated with Mercaptizol. **Discontinue treatment and contact your doctor if symptoms of vasculitis occur**, including rash, blood in urine (hematuria) or decreased urine output, shortness of breath (dyspnea) or hemoptysis (bloody cough) (see also section 4 'Side effects').

Children and adolescents
Mercaptizol is the preferred choice when a medicine for hyperthyroidism is required for a pediatric patient. For children under 6 years old please consult your doctor to consider alternative treatments, due to potential swallowing difficulties and risk of choking (see section 3 'How to use this medicine').

Tests and follow-up
- Since Mercaptizol may cause hypoprothrombinemia (decrease in the level of prothrombin, a procoagulant factor) and bleeding, prothrombin time should be monitored (in blood) during therapy with the medicine, especially before surgical procedures.
- Thyroid function tests should be monitored periodically during therapy to determine the maintenance dosage of the medicine.

Drug interactions
If you are taking, or have recently taken, other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:
- Oral anticoagulants - Mercaptizol may inhibit vitamin K activity, therefore the activity of oral anticoagulants (e.g. warfarin) may be increased. Your doctor may consider additional monitoring of coagulation profile (PT/INR), especially before surgical procedures.

- Beta-adrenergic blockers – Hyperthyroidism may cause an increased clearance of certain beta blockers medicines. Therefore, a reduced dosage of such medicines may be needed when you become euthyroid.
- Digitalis glycosides - Serum digitalis levels may be increased when you become euthyroid. Therefore, a reduced dosage of such medicines may be needed.
- Theophylline - Theophylline clearance may decrease when you become euthyroid. Therefore, a reduced dose of theophylline may be needed.

Using this medicine and food
This medicine can be taken with or without food. Ensure regular intake schedule.

Pregnancy and breastfeeding
Pregnancy
If you are planning a pregnancy, or currently pregnant, consult your doctor before using the medicine.
If you are planning a pregnancy, or become pregnant, during treatment with the medicine, inform your doctor immediately.
Rarely, Mercaptizol use may cause congenital malformations; it is therefore preferable to use other medicines in pregnant women with hyperthyroidism, particularly during organogenesis, i.e. in the first trimester of pregnancy. If nonetheless Mercaptizol therapy is necessary, the lowest possible dosage should be given.
In many pregnant women, the thyroid dysfunction diminishes as the pregnancy proceed. Consequently, a reduction of dosage may be required. In some instances, the therapy will be discontinued by your doctor several weeks or several months before delivery.

Breastfeeding
Consult your doctor if you intend to breastfeed.
Mercaptizol is excreted into breast milk. However, several studies found no effect on clinical status in nursing infants of mothers taking Mercaptizol. Your doctor should check the thyroid function at weekly or biweekly intervals.

Important information about some of this medicine's ingredients
The medicine contains lactose and sucrose. If you have been told by your doctor that you are intolerance to certain sugars, contact your doctor before using this medicine.
The medicine contains Sunset yellow (FD&C Yellow #6 Lake) which may cause allergic reactions.

3. How to use this medicine?
Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about the dosage and treatment regimen of this medicine.
The dosage and treatment regimen will be determined only by your doctor.
Mercaptizol tablets are administered orally.

The recommended dose is generally:
Adults: the initial daily dosage is 10 mg for mild hyperthyroidism, 30 to 40 mg for moderately severe hyperthyroidism, and 40 mg for severe hyperthyroidism, divided into 2 doses at 12-hour intervals. The maintenance dosage is 10 mg daily.

Children and adolescents: initially, the daily dosage is 0.4 mg/kg of body weight divided into 3 doses and given at 8-hour intervals. The maintenance dosage is approximately 1/2 of the initial dose.

Mercaptizol should be used in children 6 years of age and older due to potential swallowing difficulties and risk of choking in younger children*.*
For children under 6 years old, alternative treatments should be considered*.*

In adults and children, when the required initial or maintenance dosage is less than 10 mg, alternative treatment options should be considered.

Do not exceed the recommended dose.

- The tablet can be halved for partial dose to be taken each time or crushed.
- Swallow the medicine with a small amount of water.

If you have accidentally taken a higher dose, or if a child has accidentally swallowed some medicine, refer to the doctor or a hospital emergency room immediately and bring the medicine package with you.
Symptoms of overdose may include nausea, vomiting, epigastric distress, headache, fever, joint pain, pruritus, and edema. Aplastic anemia (decrease in blood cell count) or agranulocytosis (severe deficiency of white blood cells called neutrophils) may develop within hours to days. Less common effects include hepatitis, nephrotic syndrome (due to damage to kidneys), exfoliative dermatitis, neuropathy (peripheral nervous system disorder), CNS stimulation or depression.

If you forget to take the medicine at the scheduled time, consult your doctor.

Adhere to the treatment as recommended by your doctor.
Even if your health improves, do not stop taking this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose <u>every time</u> you take a medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. <u>Side effects</u>

Like with all medicines, using Mercaptizol may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Stop using the medicine and contact your doctor immediately in case of:

- Severe deficiency of white blood cells called neutrophils (agranulocytosis). Symptoms may include any evidence of illness particularly fever, sore throat, rash, headache and general malaise.
- Aplastic anemia (decrease in blood cell count).
- Suspected vasculitis (inflammation of blood vessels). Cases of vasculitis resulting in severe complications have been reported in patients receiving Mercaptizol therapy. These cases of vasculitis include: leukocytoclastic cutaneous vasculitis, acute kidney injury and glomerulonephritis, alveolar/pulmonary hemorrhage, CNS vasculitis, and a disease of the peripheral nervous system (neuropathy). Vasculitis is typically associated with the presence of anti-neutrophilic cytoplasmic antibodies (ANCA) (also see 'Special warnings about using this medicine' in section 2).
- Clinically significant evidence of liver abnormality. Symptoms of liver dysfunction include, among others, anorexia, pruritus, right upper quadrant abdominal pain.

Contact your doctor immediately if you experience any of the following side effects:

- Inhibition of myelopoiesis, including granulocytopenia (decrease in white blood cells called granulocytes), thrombocytopenia (decrease in platelets).
- Fever.
- Lupus-like syndrome.
- Insulin autoimmune syndrome (a syndrome in which the body creates antibodies against insulin), which can result in hypoglycemic coma due to low blood sugar levels.
- Hepatitis. Symptoms may include jaundice (which may persist for several weeks after discontinuation of the medicine).
- Inflammation of tissues surrounding the arteries (periarteritis).
- Hypoprothrombinemia (abnormally low levels of the coagulation factor prothrombin).
- Nephritis (rare).
- Acute pancreatitis.

Additional side effects:

- Skin rash, urticaria, nausea, vomiting, epigastric distress, arthralgia, paresthesia, loss of taste, abnormal hair loss, myalgia, headache, pruritus, drowsiness, neuritis, edema, vertigo, skin pigmentation, jaundice, salivary gland diseases, lymph node diseases.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
  Storage conditions
- Store below 25˚C in a cool and dark place.
- Do not throw away any medicine via wastewater or household waste. Ask the pharmacist how to throw away mmedicines you no longer use. These measures will help protect the environment.

6. Additional information:

In addition to the active ingredient, this medicine also contains:

Lactose monohydrate, calcium phosphate dibasic anhydrous, corn starch, confectioner's sugar (97% sucrose, 3% starch), talc, compressible sugar, FD&C Yellow #6 Lake

What the medicine looks like and contents of the pack:
A round, flat, peach-colored tablet, with a score line on one side.
The tablets are packed in a blister. Each pack contains 20 or 30 tablets.
Not all pack sizes may be marketed.

Manufacturer's and Registration holder's name and address: Taro Pharmaceutical Industries Ltd., 14 Hakitor St., Haifa Bay 2624761, Israel.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 014-89-24453-00

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